

**WHAT IS CLAIMED IS:**

1. A method for screening for diabetes comprising:
  - a) obtaining sample nucleic acid from an animal; and
  - b) analyzing the nucleic acid to detect a polymorphism in a calpain-encoding

5 nucleic segment;

wherein a polymorphism in the calpain-encoding nucleic acid is indicative of a propensity for type 2 diabetes mellitus.

2. The method of claim 1, wherein the calpain-encoding nucleic acid is a calpain 10-encoding nucleic acid.

3. The method of claim 2, wherein the calpain-encoding nucleic acid is DNA.

4. The method of claim 3, wherein the DNA is a cDNA encoding a calpain.

5. The method of claim 3, wherein the DNA encodes a calpain gene.

6. The method of claim 5, wherein the DNA encodes a *CAPN10* gene.

- 20 7. The method of claim 1, wherein the nucleic acid is a encodes a calpain 10 polypeptide.

- 25 8. The method of claim 1, wherein the step of analyzing the calpain-encoding nucleic acid comprises sequencing the calpain-encoding nucleic acid to obtain a sequence.

9. The method of claim 8, wherein the obtained sequence is compared to a known nucleic acid sequence of a calpain gene.

10. The method of claim 8, wherein the step of analyzing the nucleic acid comprises PCR, an RNase protection assay, or an RFLP procedure.
- 5 11. A method of regulating diabetes in an animal comprising the step of modulating calpain function in the animal.
12. The method of claim 11, further comprising the step of diagnosing an animal with diabetes via analysis of a calpain-encoding nucleic acid sequence.
- 10 13. The method of claim 12, wherein the calpain-encoding sequence is a calpain 10-encoding sequence.
- 15 14. The method of claim 11, wherein the step of modulating calpain function comprises providing a calpain polypeptide to the animal.
- 15 15. The method of claim 14, wherein the provision of an calpain polypeptide is accomplished by inducing expression of an calpain polypeptide.
- 20 16. The method of claim 14, wherein the provision of an calpain polypeptide is accomplished by a method comprising introduction of an calpain-encoding nucleic acid to the animal.
- 25 17. The method of claim 11, wherein the step of modulating calpain function in the animal comprises providing a modulator of calpain function to the animal.
18. A method of screening for modulators of calpain function comprising the steps of:
- 30 a) obtaining an calpain polypeptide;
- b) determining a standard activity profile of the calpain polypeptide;
- c) contacting the calpain polypeptide with a putative modulator; and
- d) assaying for a change in the standard activity profile.

19. The method of claim 18, wherein the calpain polypeptide is a calpain 10 polypeptide.
- 5 20. The method of claim 18, wherein obtaining the calpain polypeptide comprises expressing the polypeptide in a host cell.
21. The method of claim 20, wherein the calpain polypeptide is isolated away from the host cell prior to contacting the calpain polypeptide with the putative modulator.
- 10 22. An isolated and purified polynucleotide comprising a calpain 10-encoding sequence.
- 15 23. The polynucleotide of claim 22, comprising a sequence encoding any of calpain 10a, calpain 10b, calpain 10c, calpain 10d, calpain 10e, calpain 10f, calpain 10g, calpain 10h, or mouse calpain 10.
- 20 24. The polynucleotide of claim 23, further defined as encoding a calpain having an amino acid sequence as set forth in SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, or SEQ ID NO:18..
- 25 25. The polynucleotide of claim 22, wherein the calpain 10-encoding nucleic acid sequence has a sequence of set forth in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, or SEQ ID NO:19.
26. An isolated and purified calpain 10 polypeptide.

27. The polypeptide of claim 26, further defined as any of calpain 10a, calpain 10b, calpain 10c, calpain 10d, calpain 10e, calpain 10f, calpain 10g, calpain 10h, or mouse calpain 10.

5 28. The polypeptide of claim 27, having an amino acid sequence as set forth in SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, or SEQ ID NO:18..

29. A method of obtaining a calpain 10 polypeptide comprising:

- 10 a) obtaining a calpain 10 encoding-polynucleotide;  
b) inserting the obtained polynucleotide into a host cell; and  
c) culturing the host cell under conditions sufficient to allow production of  
the calpain 10-encoding polypeptide;

wherein a calpain 10 polypeptide is thereby obtained.

15 30. The method of claim 29, comprising the step of isolating the calpain 10 polypeptide from the host cell.

20 31. A method of modulating an insulin secretory response in an animal comprising the step of modulating calpain function in the animal.

32. The method of claim 31, wherein the step of modulating calpain function in the animal comprises providing a modulator of calpain function to the animal.

25 33. The method of claim 32, wherein the modulator of calpain function is an agonist or antagonist of a calpain polypeptide.

34. The method of claim 33, wherein the modulator of calpain function is an inhibitor of a calpain polypeptide.

35. A method of modulating insulin mediated glucose transport in an animal comprising the step of modulating calpain function in the animal.
- 5 36. The method of claim 35, wherein the step of modulating calpain function in the animal comprises providing a modulator of calpain function to the animal.
37. The method of claim 36, wherein the modulator of calpain function is an agonist or antagonist of a calpain polypeptide.
- 10 38. The method of claim 37, wherein the modulator of calpain function is an inhibitor of a calpain polypeptide.
- 15 39. A method of treating diabetes in an animal comprising the step of modulating calpain function in the animal.
40. The method of claim 39, wherein the step of modulating calpain function in the animal comprises providing a modulator of calpain function to the animal.
- 20 41. The method of claim 40, wherein the modulator of calpain function is an agonist or antagonist of a calpain polypeptide.
42. The method of claim 41, wherein the modulator of calpain function is an inhibitor of a calpain polypeptide.
- 25 43. A method of treating diabetes by modulating the function of one or more calpains in at least one of a  $\beta$ -cell, muscle cell, or fat cell with a modulator of calpain function.
44. The method of claim 43, wherein the modulator of calpain function is an agonist or antagonist of a calpain polypeptide.

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45. The method of claim 44, wherein the modulator of calpain function is an inhibitor of a calpain polypeptide.
46. The method of claim 43, further defined as a method comprising inhibiting calpain activity in a  $\beta$ -cell with a modulator of calpain function.
- 5 47. The method of claim 43, further defined as a method comprising stimulating calpain activity in a muscle cell or fat cell with a modulator of calpain function.
- 10 48. The method of claim 43, further defined as a method comprising stimulating calpain activity in a fat call or muscle cell with a modulator of calpain function and inhibiting calpain activity in a  $\beta$ -cell with a modulator of calpain function.

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